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APPLICATION NO.	FII	LING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
10/618,481	0	7/11/2003	Tony Hollingsworth	NE-0004	8213
7:	590	03/17/2006		EXAM	INER
Jane Massey 1	Licata			JOYCE, CA	THERINE
Licata & Tyrre 66 E. Main Stre				ART UNIT	PAPER NUMBER
Marlton, NJ (1642	
				DATE MAILED: 03/17/2000	6

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(a)
	Application No.	Applicant(s)
Office Action Summary	10/618,481	HOLLINGSWORTH ET AL.
omce Action Guinnary	Examiner	Art Unit
The MAIL ING DATE of this and a single state of the same of the sa	Catherine M. Joyce	1642
The MAILING DATE of this communication app Period for Reply	lears on the cover sneet with the c	orrespondence address
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING D/ - Extensions of time may be available under the provisions of 37 CFR 1.1: after SIX (6) MONTHS from the mailing date of this communication. If NO period for reply is specified above, the maximum statutory period v - Failure to reply within the set or extended period for reply will, by statute Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 36(a). In no event, however, may a reply be tim will apply and will expire SIX (6) MONTHS from a cause the application to become ABANDONE!	I. lely filed the mailing date of this communication. O (35 U.S.C. § 133).
Status		
1) Responsive to communication(s) filed on 12 Ja	anuary 2006.	
	action is non-final.	
3) Since this application is in condition for allowar		secution as to the merits is
closed in accordance with the practice under E	•	
Disposition of Claims		
4) Claim(s) 1-3 is/are pending in the application.		
4a) Of the above claim(s) <u>2</u> is/are withdrawn fro	om consideration.	
5) Claim(s) is/are allowed.		
6)⊠ Claim(s) <u>1 and 3</u> is/are rejected.		
7) Claim(s) is/are objected to.		
8) Claim(s) are subject to restriction and/o	r election requirement.	
Application Papers		
9) The specification is objected to by the Examine	er.	
10) The drawing(s) filed on is/are: a) acc		Examiner.
Applicant may not request that any objection to the	drawing(s) be held in abeyance. See	e 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correct	ion is required if the drawing(s) is obj	ected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Ex	caminer. Note the attached Office	Action or form PTO-152.
Priority under 35 U.S.C. § 119	•	
12) ☐ Acknowledgment is made of a claim for foreign a) ☐ All b) ☐ Some * c) ☐ None of:		-(d) or (f).
1. Certified copies of the priority document		
2. Certified copies of the priority document		
3. Copies of the certified copies of the prior	- ·	ed in this National Stage
application from the International Bureau	• • • • • • • • • • • • • • • • • • • •	d
* See the attached detailed Office action for a list	or the certified copies not receive	u.
AMosh-road/s)		
Attachment(s) 1) Notice of References Cited (PTO-892)	4) Interview Summary	(PTO-413)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Da	nte
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date	5)	atent Application (PTO-152) <u>2 App. B(2p)</u> .

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Art Unit: 1642

1. Claims 1-3 are pending, and claim 2 is withdrawn from consideration as being drawn to a non-elected invention

- 2. Claims 1 and 3 are under examination.
- 3. Applicant's election with traverse of Group I, claims 1 and 3, in the reply filed on January 12, 2006 is acknowledged. The traversal is on the ground(s) that searching Groups I and II together would not pose a search burden. This argument is not found persuasive because, while the searches for the inventions of groups I and II would be overlapping they would not be coextensive. The search for the invention of group I would include a search for a composition comprising the recited polypeptide, whatever the intended use of the composition, whereas a search for the method of method of group II would include a search on all methods of treating cancer with MUC-1 compositions, including DNA compositions. Therefore, a search for one group would not be coextensive with a search for the other group. Thus, the requirement for restriction is deemed proper and is therefore made FINAL.
- 4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Art Unit: 1642

5. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoover (1993, J. Clin. Oncol. 11(3):390-9), as evidenced by Byrd (2004, Cancer and Metastasis Review 23:77-99).

The claims are drawn to a composition for preventing or treating cancer in a subject comprising at least a portion of a MUC1 cytoplasmic tail peptide of SEQ ID NO:1 (claim 1), wherein at least a portion of a MUC1 cytoplasmic peptide of SEQ ID NO:1 comprises a vaccine.

It is noted that the recitation of "for preventing or treating cancer" in claim 1 and "comprises a vaccine" are merely suggestive of an intended use and are not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredient *per se*, which is "at least a portion of a MUC1 cytoplasmic tail peptide of SEQ ID NO:1".

Hoover et al. describe clinical trials wherein patients with Dukes' B2 or C3 were treated with an autologous tumor-bacillus Calmette-Guerin (BCG) vaccine composition (abstract). The vaccine compositions comprised a patient's autologous tumors cells combined with bacillus Calmette-Guerin. As evidenced by Byrd et al., MUC-1 is expressed in colon cancer cells (page 82). Thus, the autologous tumor cell vaccine compositions of Hoover would comprise a cytoplasmic tail peptide of SEQ ID NO:1. Thus, all of the claim limitations are met.

6. Claims 1 and 3 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 02/058450.

The claims are drawn to a composition for preventing or treating cancer in a subject comprising at least a portion of a MUC1 cytoplasmic tail peptide of SEQ ID NO:1 (claim 1), wherein at least a portion of a MUC1 cytoplasmic peptide of SEQ ID NO:1 comprises a vaccine.

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Art Unit: 1642

It is noted that the recitation of "for preventing or treating cancer" in claim 1 and "comprises a vaccine" are merely suggestive of an intended use and are not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredient *per se*, which is "at least a portion of a MUC1 cytoplasmic tail peptide of SEQ ID NO:1".

WO 02/058450 describes a composition comprising a polypeptide having the amino acid sequence of SEQ ID NO:1 of the instant application, which is a molecule comprising at least a portion of cytoplasmic tail, a composition comprising a polypeptide having the amino acid sequence of amino acid residues 1 to 42 of SEQ ID NO:1 of the instant application, which is a molecule comprising at least a portion of the cytoplasmic tail, and a composition comprising a polypeptide having the amino acid sequence of amino acid residues 22 to 72 of SEQ ID NO:1 of the instant application, which is a molecule comprising at least a portion of the cytoplasmic tail (page 46, Example 6, and Figure 7A). A comparison of the cited sequences with SEQ ID NO:1 is included herewith as an Appendix A to this Action.

7. Claims 1 and 3 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,548,643.

The claims are drawn to a composition for preventing or treating cancer in a subject comprising at least a portion of a MUC1 cytoplasmic tail peptide of SEQ ID NO:1 (claim 1), wherein at least a portion of a MUC1 cytoplasmic peptide of SEQ ID NO:1 comprises a vaccine.

It is noted that the recitation of "for preventing or treating cancer" in claim 1 and "comprises a vaccine" are merely suggestive of an intended use and are not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredient *per se*, which is "at least a portion of a MUC1 cytoplasmic tail peptide of SEQ ID NO:1".

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US Patent 6,548,643 teaches conjugates between an antigen and a carbohydrate polymer, wherein the conjugates may be immunogenic vaccines, and wherein the conjugates may especially comprise contain one or more repeated subunits of human mucin or non-repeated repeated regions of human mucin (abstract). US Patent 6,548,643 also teaches that immunogenic peptides may be derived from the extracellular region or intracellular region of MUC1 (column 8, lines 14-16), and that preferred peptides comprises amino acids 1-21 or 35-54 of the intracellular portion of MUC 1 (i.e. of SEQ ID NO:1 of the instant application) (columns 7 and 8, lines 25-43 and SEQ ID NOs:16 and 17), which are at least a portion of cytoplasmic tail. A comparison of the cited sequences with SEQ ID NO:1 is included herewith as an Appendix to this Action. Thus, all of the claim limitations are met.

8. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine M. Joyce whose telephone number is 571-272-3321. The examiner can normally be reached on Monday thru Friday, 10:15 - 6:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Ungar Susan Ungar Primary Patent Examiner Art Unit: 1642

Catherine Joyce Examiner Art Unit 1642

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Minimum DB
Maximum DB
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Maximum Match 100%
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395
                                                                                                                             A_Geneseq_21:*
1: geneseqp1980s:*
2: geneseqp1990s:*
                                                                                                                                                                                                                                                                                                                                                                      2443163 segs, 439378781 residues
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                                                                                                                                                                                                                                                                                                                                                                                                                                                             1 CQCRRKNYGQLDIFPARDTY......NGGSSLSYTNPAVAAASANL 72
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          February 3,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    GenCore version 5.1.7
Copyright (c) 1993 - 2006 Biocceleration Ltd.
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geneseqp2002s:*
geneseqp2005s:*
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159.774 Million cell updates/sec
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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

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	150	136	127	110	93	72	1255	1255	1255	1255	1255	1255	1255	1255	1255	1255	1255	1255	863	312	275	171	146	72	Length
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	ADI57762	AEC04627	ADI57781	ADI57780	AAY71023	ADU15747	AEC04621	AEB87750	AEA63704	AEA24480	ADY53504	ADQ29694	ADE54622	ADD45111 ·	ABR92124	ABR47537	ABB82568	ABP56040	ADY53535	AAU84810	ADY53533	ADY53532	ADY53531	ABB79839	ID
	Adi57762 Human bre	Aec04627 Human bre	Adi57781 Human bre	Adis7780 Human bre	Aay71023 Human Muc	Adu15747 Full leng	Aec04621 Human bre	Aeb87750 Human muc	Aea63704 Human muc	Prote	Ady53504 Full-leng			۲	Abr92124 Human cer	Abr47537 Breast ca		0	Ady53535 Truncated	Aau84810 Human MUC	Ady53533 Truncated	Ady53532 Truncated	1 Trunc	Abb79839 MUC1 cyto	Description

					4
	ALIGNMENTS				
Aar89420 Mucin-der		255	•	391	45
0	00	252	•	391	44
Aae37798 Human muc		252	•	391	43
Ada50577 Mucin 1 (0	252	99.0	391	42
	7	249	•	391	41
Adi57768 Human bre	œ	241	•	391	40
Ade48140 MUC1/V pr		240	•	391	39
Aar89422 Mucin-der	2 AAR8942	240	•	391	38
Aar89423 Mucin-der	2 AAR8942	239	•	391	37
	9	233	•	391	36
	8 ADI5777	232	•	391	35 5
Adis7756 Human bre	8	230	•	391	34
Adj68550 Human hea	7	230	•	391	33
	σ	230	•	391	32
Aay71029 Ubiquitin	w	215	•	391	31
Human b	ø	203	•	391	30
Human	œ	180	•	391	29
Adi57763 Human bre	œ	168	•	391	28
Aec04624 Human bre	9	166	•	391	27
Aec04626 Human bre	9	159	•	391	26
Aec04625 Human bre		157		391	25

```
RESULT 1
ABB79839
ID ABB7
XX
AC ABB7
XX
AC ABB7
XX
XX
XX
    SXXXX
Identifying compounds that inhibit the binding of MUC1 to a tumor progressor, or inhibits the phosphorylation of MUC1 by the tumor progressor, by contacting the MUC1 test agent with the tumor progressor
                                                                                                                                                                                                                           Binding-site
                                                                                                                                                                                                                                                                                                        Modified-site
                                                                                                                                                                                                                                                                                                                                                                                                                                  MUC1 cytoplasmic domain.
                                                                                                               22-DEC-2000; 2000US-0257590P.
27-JUL-2001; 2001US-0308307P.
                                                                                                                                                                     01-AUG-2002.
                                                                                                                                                                                                                                               Binding-site
                                                                                                                                                                                                                                                                                  Modified-site
                                                                                                                                                                                                                                                                                                                             Binding-site
                                                                                                                                                                                                                                                                                                                                                                Key
                                                                                                                                                                                                                                                                                                                                                                                      Homo sapiens.
                                                                                                                                                                                                                                                                                                                                                                                                            MUC1; mucin;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                              ABB79839;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  ABB79839 standard; protein; 72 AA.
                                              WPI; 2002-666881/7I.
                                                                    Kufe DW;
                                                                                                                                               26-DEC-2001; 2001WO-US049923
                                                                                                                                                                                         WO200258450-A2
                                                                                                                                                                                                                                                                                                                                                    Peptide
                                                                                                                                                                                                                                                                                                                                                                                                                                                        25-NOV-2002
                                                                                        (DAND ) DANA
                                                                                         FARBER CANCER INST INC
                                                                                                                                                                                                                                                                                                                                                                                                            human; antitumour; cytostatic; cancer; gene therapy.
                                                                                                                                                                                                                                                                                                                                                                                                                                                        (first entry)
                                                                                                                                                                                                              50. .59
/note= "beta-catenin binding site"
                                                                                                                                                                                                                                                                                   /note= "Phosphorylated by protein kinase C-delta"
44
                                                                                                                                                                                                                                                            beta"
                                                                                                                                                                                                                                      /note=
                                                                                                                                                                                                                                                                      note= "Phosphorylated by glycogen synthase kinase
                                                                                                                                                                                                                                                                                                                   note=
                                                                                                                                                                                                                                                                                                                                        /note= "peptide specifically described in Claim 56"
                                                                                                                                                                                                                                                                                                                                                             Location/Qualifiers
                                                                                                                                                                                                                                                 .49
                                                                                                                                                                                                                           . 59
                                                                                                                                                                                                                                      "c-Src binding site"
                                                                                                                                                                                                                                                                                                                  "glycogen synthase kinase 3-beta binding site"
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in the presence of the test compound

English

tetrapeptide sequence which is portion of MUC1 receptor that functions as growth factor receptor, useful for diagnosing and treating cancer.

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RESULT 2
AD753531
ID AD75
XX A
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Best Local (
                                                                                  N-PSDB; ADY53536.
Antibody or antigen-binding fragment that specifically binds
                                                                                                                    WPI; 2005-214228/22.
                                                                                                                                                                                                  Bamdad CC;
                                                                                                                                                                                                                                                                                                                                                        26-AUG-2003; 2003US-0498260P
                                                                                                                                                                                                                                                                                                                                                                                                                                      26-AUG-2004; 2004WO-US027954
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    WO2005019269-A2.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Homo sapiens
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             antibody; antigen-binding fragment; MUC1 receptor;
growth factor receptor; cancer; cytostatic.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Truncated MUC1 growth factor receptor isoform, SEQ ID
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                19-MAY-2005 (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   ADY53531;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     ADY53531 standard; protein; 146
                                                                                                                                                                                                                                                                             (MINE-) MINERVA BIOTECHNOLOGIES
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           61
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      1 CQCRRKNYGQLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSY 60
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          TNPAVAAASANL 72
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The invention relates to a novel antibody or its antigen-binding fragment CC that specifically binds to a tetrapeptide sequence which is a portion of CC a MUC1 receptor that functions as a growth factor receptor. The invention CC further comprises a series of compositions, methods, kits, articles and CC species associated primarily with the diagnosis and/or treatment of cell CC proliferation, specifically cancer. The antibody or its antigen-binding CC fragment is useful for treating a subject having cancer caused by CC aberrant expression of MUC1, which involves administering the antibody or its antigen-binding fragment in an amount effective to block interaction CC in antigen-binding fragment in an amount effective to block interaction CC in the cell surface after cleavage of the receptor, or in an amount CC effective to reduce shedding of an interchain binding region of the MUC1 receptor. The antibody or its antigen-binding CC colorectal, pancreas and brain. The antibody or its antigen-binding CC colorectal, pancreas and brain. The antibody or its antigen-binding CC subject suspected of having cancer with the antibody or its antigen-colorectal suspected of having cancer with the antibody or its antigen-colorectal suspected of having cancer with the antibody or its antigen-colorectal susface, and determining the amount of the antibody or its antigen-colorectal susface, and determining the amount of the antibody or its antigen-color the aggressiveness of a cancer. This sequence of absence of cancer of cancer or the aggressiveness of a cancer. This sequence represents a truncated MUC1 growth factor receptor isoform of the invention.
Sequence 146
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Claim 68; SEQ ID NO 37; 204pp; English
   A
A
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#X#X5555555555555555555555555555555

Sequence 72 AA;

Length 72;

cancer cell that expresses MUC1

CC The present sequence is the cytoplasmic domain (CD) of mucin MUC1, a CC glycoprotein expressed aberrantly at high levels over the surface of CC breast, prostate, lung and other types of carcinoma cells. MUC1 binds via CC its CD to c-Src, epidermal growth factor receptor (EGF-R), pl20ctn and CC protein kinase C (PKC)-delta. c-Src, EGF-R and PKC-delta phosphorylate CC the MUC1 CD, leading to enhanced binding of PKC-delta phosphorylate CC phosphorylation by EGF-R leads to enhanced binding of c-Src to MUC1. The CC invention features methods of identifying compounds that inhibit (a) the binding of MUC1 to a tumour progressor (e.g. beta-catenin, c-Src, EGF-R, CC pl20ctn, or PKC-delta) and/or (b) phosphorylation of MUC1 by tumour progressors with kinase activity (e.g. c-Src, EGF-R, or PKC-delta). The CC progressors with kinase activity (e.g. c-Src, EGF-R, or PKC-delta). The CC progressors with kinase activity (e.g. c-Src, EGF-R, or PKC-delta). The CC inding to, and phosphorylation of, MUC1 by glycogen synthase kinase 3 compounds that enhances binding to, and phosphorylation of, MUC1 by glycogen synthase kinase 3 compounds that contain to a tumour progressor in a cancer cell, especially a breast cancer cell, or a lung, colon, pancreatic, renal, stomach, liver, bone, CC cancer cell (e.g. leukaemia, prostate, cryoical, vaginal, or bladder cancer cell. Covarian, testicular, prostate, prostate, cryoical, vaginal, or bladder cancer cell. Cancer cell that expresses mIC1 cancer cell that expresses or cancer cell.

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                                                                                      Matches
                                                                                                 Query Match
Best Local :
                                                                                               Local
135
                                         75
                  61 TNPAVAAASANL 72
                                                               1 CQCRRKNYGQLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSY 60
                                                                                      72; Conservative
                                                                                               Similarity
                                                                                              100.0%;
                                                                                     <u>,</u>
                                                                                   Score 395; DB 9;
Pred. No. 2.1e-42;
; Mismatches 0;
                                                                                                          Length 146;
                                                                                     Indels
                                                                                    ç,
                                          134
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RESULT 3
ADY53532
antibody; antigen-binding fragment; MUC1 receptor;
growth factor receptor; cancer; cytostatic.
                                                                           Truncated MUC1 growth factor receptor isoform, SEQ ID 38.
                                                                                                                               19-MAY-2005
                                                                                                                                                                                  ADY53532;
                                                                                                                                                                                                                                   ADY53532 standard; protein; 171 AA
                                                                                                                               (first entry
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03-MAR-2005.
                         WO2005019269-A2.
                                                     Homo sapiens
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26-AUG-2003; 2003US-0498260P 26-AUG-2004; 2004WO-US027954.

(MINE-) MINERVA BIOTECHNOLOGIES CORP

Bamdad CC WPI; 2005-214228/22

US-09-134-916A-2

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Sequence 2, Applic
Patent No. 6328956
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           APPLICATION NUMBER: US/08/479,537
FILING DATE: 07-JUN-1995
APPLICATION NUMBER: FR 90/13101
FILING DATE: 23-OCT-1990
PRIOR APPLICATION DATA:
APPLICATION NUMBER: WO PCT/FR91/00835
FILING DATE: 23-OCT-1991
PRIOR APPLICATION DATA:
APPLICATION NUMBER: US 08/039,320
FILING DATE: 04-APR-1993
PRIOR APPLICATION NUMBER: US 08/039,320
FILING DATE: 14-APR-1993
PRIOR APPLICATION NUMBER: US 08/403,576
FILING DATE: 14-MAR-1995
ATTORNEY/AGENT INFORMATION:
APPLICATION TONEY AGENT INFORMATION:
                                                                                                                                                                                                                                                                                                                                                                                                              TELEFAX: (703) 836-2021 INFORMATION FOR SEQ ID NO: 2:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 GENERAL INFORMATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                  NAME: Teskin, Robin L.
REGISTRATION NUMBER: 35,030
REFERENCE/DOCKET NUMBER: 01
TELECOMMUNICATION INFORMATION:
TELEPHONE: (703) 836-6620
                                                                                                                                                                                                                                                                                                                                                                                        SEQUENCE CHARACTERISTICS:
                                                                                                                                              LOCATION: 128..1899
OTHER INFORMATION:
OTHER INFORMATION:
OTHER INFORMATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Patentin Release #1.0, Version #1.30
CURRENT APPLICATION DATA:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   PRIOR APPLICATION DATA:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                ZIP: 22313-1404
COMPUTER READABLE FORM:
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       APPLICANT:
                                                                                                                                                                                                                                                                               OLECULE TYPE: peptide
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   NUMBER OF SEQUENCES: 5
                            OTHER INFORMATION: OTHER INFORMATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        TITLE OF INVENTION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    TITLE OF INVENTION:
      OTHER INFORMATION:
                                                                                                                                                                                                                                                                                                                       TYPE: amino acid
STRANDEDNESS: sir
                                                                                           NAME/KEY:
                                                                                                                                 OTHER INFORMATION:
                                                                                                                                                                                                               NAME/KEY: Peptide
LOCATION: 128..1899
                                                                                                                                                                                                                                                                                                        TOPOLOGY:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         FILING DATE:
CLASSIFICATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                STREET: P.O. BOX
CITY: Alexandria
                                                                     LOCATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    APPLICATION NUMBER:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           STATE: Virginia
COUNTRY: United States
                                                                                                                                                                                                                                                                                                                                                                        ENGTH:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  ADDRESSEE:
                                                                                                                                                                                                                                                                                                                                                                  2035 amino acids
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        KIENY, Marie-Paule
LATHE, Richard
HAREUVENI, Mara
                                                                                                                                                                                                                                                                                                      linear
                                                                                         Peptide
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           BURNS, DOANE, SWECKER & MATHIS, L.L.P
O. Box 1404
                                                                                                                                                                                                                                                                                                                       single
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OR PREVENTION OF A MALIGNANT TUMOR
                                                                                                                            /note= "The amino acids spanning
128 to 1899 constitute a repeated region wherein the
20 amino acids, 17 of which are fixed. The number of
repeats varies from 1 to 40."
/note= "Amino acid 134 is X1 = Xaa
Xaa Xaa which is the codon for Pro or Ala wherein Pro
CCC, CCA, or CCG; and Ala = GCT, GCC, GCA, or GCG."
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US-09-593-870A-17

sequence 17, Application US/09593870A
Patent No. 6548643

GENERAL INFORMATION:
APPLICANT: APOSTOlopoulos, V
APPLICANT: Apostolopoulos, V
APPLICANT: Pietersz, Geoff A

APPLICANT: Apostolopoulos, Vasso
APPLICANT: Pietersz, Geoff Allan
TITLE OF INVENTION: Antigen Carbohydrate Compounds and Their
TITLE OF INVENTION: Use in Immunotherapy

FILE REFERENCE: 2368-McKenzie

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US-09-593-870A-16
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                                                                                                                                                                                                          FILE REFERENCE: 2368-MCKenzie
CURRENT EPILICATION NUMBER: US/09/593,870A
CURRENT FILING DATE: 2000-06-14
PRIOR APPLICATION NUMBER: 09/223,043
PRIOR FILING DATE: 1998-12-30
NUMBER OF SEQ ID NOS: 69
SOFTWARE: FastSEQ for Windows Version 3.0
SEQ ID NO 16
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     US-09-134-916A-2
                                                                       Matches
                                                                                                        Query Match
                                                                                                                                                                                                                                                                                                                                                                                                                          APPLICANT: McKenzie,
                                                                                       Best Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Patent No. 6548643
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Matches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Query Match
                                                                                                                                                                                                                                                                                                                                                   APPLICANT: Apostolopoulos, Vasso
APPLICANT: Pietersz, Geoff Allan
TITLE OF INVENTION: Antigen Carbohydrate Compounds and Their
TITLE OF INVENTION: Use in Immunotherapy
                                                                                                                                                         TYPE: PRT
ORGANISM: Homo sapiens
                                                                                                                                                                                             LENGTH:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           FEATURE:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      NAME/KEY:
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OTHER INFORMATION:
OTHER INFORMATION:
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OTHER INFORMATION:
OTHER INFORMATION:
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     2024 TNPAVAATSANL 2035
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       1964 CQCRRKNYGQLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSY 2023
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    61 TNPAVAAASANL 72
                                                                       21; Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           1 CQCRRKNYGQLDIFFARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSY 60
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            71;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Similarity
                                  COCREMINGOLDIFPARDTYH 21
COCKRIGNYGOLDIFPARDTYH 23
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Application US/09593870A
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Peptide
                                                                                                                                                                                                                                                                                                                                                                                                                            Ian F.C.
                                                                                     31.4%; Score 124; DB 2; 100.0%; Pred. No. 1.2e-08
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              99.0%;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    /note= "Amino acid 147 is X2 = Xaa
which is the codon for Pro or Ala wherein Pro = CCT, CCC,
or CCG; and Ala = GCT, GCC, GCA, or GCG."
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     /note= "Amino
21 amino acid
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 /note= "Amino acid 144 is Y = Xaa
which is the codon for Thr or Asn wherein Thr =
or ACG; and Asn = AAT or AAC."
                                                                     <u>.</u>
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              <u>,</u>
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Score 391; DB 2;
Pred. No. 2.2e-39;
                                                                     Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  acids 1 to 21 are precursor sequence
                                                                                                    Length 23
                                                                   0
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                                                                 Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Gaps
                                                                   0;
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Appendix B, page 1

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; TYPE: PRT; ORGANISM: Homo sapiens US-09-593-870A-48
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US-09-593-870A-48
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   ; ORGANISM: Homo sapiens US-09-593-870A-17
                                                                                                                                                                                                                                                                                                                                                                                                                                                                  밁
                                                                                                                                                                                                                                                                                                                                                                               US-08-560-005-3
                                                                                                                                                                                                                                                                                                                                 Sequence 3, Application US/08560005
Patent No. 6001354
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             SOPTWARE: FastSEQ for Windows Version 3.0 SEQ ID NO 48 LENGTH: 21
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        APPLICANT: McKenzie, Ian F.C.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Sequence 48, Application US/09593870A Patent No. 6548643
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Query Match 27.1
Best Local Similarity 100.
Matches 20; Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    SOFTWARE: FastSEQ for Windows Version SEQ ID NO 17
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Matches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Query Match
Best Local Similarity
                                                                                                                                                                            GENERAL INFORMATION:

APPLICANT: Pot, David A.

APPLICANT: Williams, Lewis T.

APPLICANT: Jefferson, Anne Bennett

APPLICANT: Majerus, Philip W.

TITLE OF INVENTION: No. 6001354el Grb2 Associating Protein and Nucleic TITLE OF INVENTION: Acids Encoding Therefor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              APPLICANT: Apostolopoulos, Vasso
APPLICANT: Pietersz, Geoff Allan
TITLE OF INVENTION: Antigen Carbohydrate Compounds and Their
TITLE OF INVENTION: Use in Immunotherapy
FILE REFERENCE: 2368-McKenzie
CURRENT APPLICATION NUMBER: US/09/593,870A
CURRENT FILING DATE: 2000-06-14
PRIOR APPLICATION NUMBER: 09/223,043
PRIOR FILING DATE: 1998-12-30
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         CURRENT APPLICATION NUMBER: US/09/593,870A CURRENT FILING DATE: 2000-06-14 PRIOR APPLICATION NUMBER: 09/223,043 PRIOR FILING DATE: 1998-12-30 NUMBER OF SEQ ID NOS: 69
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               NUMBER OF SEQ ID NOS:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          TYPE: PRT
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                                                                                                                        NUMBER OF SEQUENCES: 10
CORRESPONDENCE ADDRESS:
ADDRESSEE: Townsend and Townsend and Crew
COMPUTER READABLE FORM:
                                                                                CITY: San Francisco
                                                                                                      STREET:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        35 YVPPSSTDRSPYEKVSAGNG 54
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          YVPPSSTDRSPYEKVSAGNG 54
                                                               California
                                                                                                    One Market Plaza, Steuart Tower, Suite 2000
                                           USA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               27.1%; Score 107; DB 2; 1 ilarity 100.0%; Pred. No. 1.3e-06; Conservative 0; Mismatches 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      27.1%; Score 107; DB 2; 100.0%; Pred. No. 1.3e-06;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    0; Mismatches
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Sequence 3, Applic
Patent No. 6296848
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Matches
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                TELEFAX: 415-326-2422 INFORMATION FOR SEQ ID NO: 3:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     SEQUENCE CHARACTERISTICS: LENGTH: 398 amino acid
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    REGISTRATION NUMBER: 29,684
REFERENCE/DOCKET NUMBER: 23
TELECOMMUNICATION INFORMATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             SOFTWARE: PatentIn Release #1.0, CURRENT APPLICATION DATA:
                                                                                                                                                                    COMPUTER READABLE FORM:
MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
                                                                                                                                                                                                                                                                       ATTORNEY/AGENT INFORMATION: NAME: Dow, Karen B.
CLASSIFICATION:
PRIOR APPLICATION DATA:
PRIOR APPLICATION NUMBER: US 08/560,005
PILLING DATE: 17-NOV-1995
ATTORNEY/AGENT INFORMATION:
                                                                                                                SOPTWARE: PatentIn Release #1.0, CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/418,540
                                                                                                                                                                                                                                                                                                                                                                                                          APPLICANT: Pot, David A.
APPLICANT: Williams, Lewis T.
APPLICANT: Jefferson, Anne Bennett
APPLICANT: Majerus, Philip W.
TITLE OF INVENTION: No. 6296848el Grb2 Associating Protein and Nucleic
TITLE OF INVENTION: Acids Encoding Therefor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               FEATURE:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             MOLECULE TYPE: protein
                                                                                                                                                                                                                                                                                                                                                   CORRESPONDENCE ADDRESS:
ADDRESSEE: Townsend and Townsend and Crew
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               COMPUTER: IBM PC compatible OPERATING SYSTEM: PC-DOS/MS-DOS
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Local
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     LOCATION: 1..398
OTHER INFORMATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         NAME/KEY: Region
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         APPLICATION NUMBER: US/08/560,005
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     MEDIUM TYPE:
COMPUTER: II
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   LENGTH: 398 amino acids
TYPE: amino acid
TOPOLOGY: linear
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  TELEPHONE:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      CLASSIFICATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         FILING DATE:
                                                                                            FILING DATE:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          190 KNGTHLELLDTREQLKRALVERDAFIGFHEOPVTFEPTYRVTVGTTEQDGKRV-PSWTDR 248
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 249 ILYK----GDGITGLSYTNNKKAVASDHL 273
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            INFORMATION:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   44 SPYEKVSAGNGGSSLSYTNPAVAAASANL 72
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              6 KNYGQLDIFPARDT------YH--PMSEYPTYHT-----HGRYVPPSSTDR 43
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        28;
                                                                                                                                                                                                                                                         94105
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Application US/09418540
                                                                                                                                                                                                                                                                                                                                 One Market Plaza, Steuart Tower, Suite 2000
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  : 415-326-2400
415-326-2422
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Conservative
                                                                                                  14-OCT-1999
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Floppy disk
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        18.1%; Score 71.5; I
31.5%; Pred. No. 1.4;
tive 11; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     /note= "celegptase"
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            No. 1.4;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Version #1.25
                                                                                                                                                            Version #1.25
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              DB 2;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          23;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Length 398;
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